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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/176,664	10/21/1998	LAWRENCE SALKOFF	018512-00012	2149

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/176,664	Applicant(s) Salkoff et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 12, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4, 5, 8, 9, 26, 27, and 45-48* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4, 5, 8, 9, 26, 27, and 45-48* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The amendment filed 2/12/02 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (1/3/01).

3. The Declaration of Dr. Timothy Jegla has been considered and is discussed below in the Response to Applicants arguments.

4. Response to Applicants arguments

Applicant argues Slo3 potassium channel is expressed in spermatocytes and it is activated by changes in intracellular pH and membrane potential. Applicant and Dr. Timothy Jegla argue that intracellular pH has a profound effect on the viability of mammalian sperm. Applicants have submitted Exibits A and b, two references that Applicants argue alkaline pH is necessary for sperm capacitation and acrosome reaction. Applicants argue since the newly identified Slo3 is highly and specifically expressed in sperm and is activated by alkalinization, persons of skill in the art would expect that the Slo3 channel plays an important role in sperm capacitation, e.g. by increasing potassium permeability, and therefore serve as a target for candidate compounds that modulate sperm function and modulators of Slo3 channel may be used to treat infertility conditions due to Slo3's involvement in capacitation and acrosome reaction. Applicants arguments have been fully considered but not found persuasive. The Exibits provided by Applicant sperm acrosome reaction is a Ca^{2+} dependent secretory event required for fertilization (Exhibit provided by Applicant, Arnoult et al) and intracellular pH regulates several aspects of mammalian sperm function, although the

transport mechanism that control these cells is not understood sperm of many animal species must complete the acrosome reaction, a ca dependent secretory event, prior to fertilization (Exhibit provided by Applicant, Zeng et al).----Although, Slo3 potassium channel is expressed in spermatocytes and it is activated by changes in intracellular pH and membrane potential there is no disclosure in the Exibits provided that changes in intracellular pH has a profound effect on the viability of mammalian sperm due to Slo3 potassium channel. Alkaline pH is necessary for sperm capacitation and acrosome reaction, but it due to calcium channel activity (see Exibits A and B provided by Applicant) . Even though the newly identified Slo3 is highly and specifically expressed in sperm and is activated by alkalinization there is no disclosure to show it is directly the cause of or even involved in initiating sperm capacitation, e.g. by increasing potassium permeability. Persons of skill in the art may expect that the Slo3 channel plays an important role in the spermatocytes but their role is not known at present. Slo3 may serve may serve serve as a target for candidate compounds but there is no showing said compounds would modulate sperm function and that said compounds may be used to treat infertility conditions due to Slo3's involvement in capacitation and acrosome reaction. Further Specification does not disclose if proteins encoded by the polynucleotides of SEQ ID NO:2, 16 and 18 all encode functional channels. The example do not disclose which channel was sensitive to potassium since all the proteins are referred to as Slo3 without reference to SEQ ID NO:.

The rejection of record under 35 USC § 101 and 35 USC § 112, 1st paragraph is maintained and is also applied to newly Amended claim 1 because Amended claim 1 is broader in scope than before Amendment. Due to recitation of "moderate stringency hybridization conditions" the claim encompasses nucleic acids which may be completely unrelated to the polynulceotide of SEQ ID NO:2, 16 and 18. The rejection prior under 35 USC § 101 and 35 USC § 112, 1st paragraph is reiterated below but addresses newly amended claim.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 4, 5, 8, 9, 26-27, 45-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further

research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 1, 4, 5, 8, 9, 26-27, 45-48.

The claims are directed to isolated polynucleotide comprising a sequence encoding the polypeptide of: a) SEQ ID NOs: 1, 3, 16 and 18 or other proteins which have specific functional features associated with the claimed pH sensitive potassium channel.

It appears from the specification that the nucleic acid of SEQ ID NOs: 2, 17 and 19 encode full length monomer of a pH sensitive potassium channel, the monomer having a unit conductance of approximately 80-120 pS when the monomer is in a functional tetramaric form, capable of transporting potassium ions, having increased potassium ion transporting activity above an intracellular pH of 7.1, specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1, 16 or 18 (encoded by the DNA of SEQ ID NOS:2, 17 and 19). The specification further provides a partial sequence for a nucleic acid (SEQ ID NO:4) encoding the partial sequence of the polypeptide of SEQ ID NO:3. The disclosure is

confucing because it not clearif all the sequences, ie. DNA of SEQ ID NOS:2, 17 and 19 encode functional polypeptide.

The applicant has mentioned general functional activities which may be applicable to known pH sensitive potassium channel proteins but not disclosed the function associated with the specific proteins encoded by the claimed nucleic acids. The specification discloses potassium channels are found in a wide variety of animal cells and "channels regulating these currents open and allow the escape of potassium under certain conditions. Potassium channels are also disclosed to be "involved in diverse functions such as regulating arteriolar smooth tone", tuning of hair cell frequency, and modulation of transmitter release at nerve terminals". Although the claimed polynucleotides of instant application encode potassium channels the specific result of changing potassium flux is not known. The specification discloses the Slo3, pH sensitive potassium channels can be used in screening inhibitors and activators, in methods of identifying homologs, in cellular transfection, and gene therapy. In light of the specification the skilled artisan can speculate that the polypeptide encoded by disclosed polynuceotides, and nucleic acid that hybridize to the disclosed nucleic acids of SEQ ID NOS:2, 17 and 19, belong to the pH sensitive potassium channel proteins. However, apart from the disclosure of SEQ ID NOS:1-4 and 16-18 no other disclosure is provided within the instant specification on what the functional features the protein encoded by the claimed polynucleotides, nor are any disease states disclosed that are directly related to its dysfunction.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptides of instant invention, or polynucleotides that encode them, are known, and the

hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the claimed nucleic acids, useful to identify drugs that affect said proteins and modulate their activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using claimed polynucleotides. Thus the corresponding asserted utilities are essentially methods of using the claimed polynucleotide to identify other nucleic acids that hybridize to said polynucleotide, or to isolate disease states associated with polypeptide disfunction, and as targets for drug discovery. Therefore the asserted utilities are essentially methods of isolating, testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating, isolating or testing for compounds that interact with the claimed polynucleotide, or encoded polypeptide, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polynucleotides, further experimentation is necessary to attribute a utility to the claimed polypeptides and polynucleotide. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but

compensation for its successful conclusion."). Accordingly, the instant specification provides insufficient guidance on "how to use" the claimed polynucleotide of instant invention. Likewise, the instant specification provides insufficient guidance on "how to use" vector containing claimed nucleic acid and cell containing said vector.

Claim Rejection, 35 U.S.C. 112, first paragraph

4. Claims 1, 4, 5, 8, 9, 26-27, 45-48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the nulceic acids of instant invention, further experimentation is necessary to attribute a utility to the claimed polynucleotides.

Amended claims 1, 4, 5, 8, 9, 26-27, 45-48 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. This rejection is maintained for reasons set forth above in the statement of the grounds of rejection under 35 U.S.C. §101. Further due to inclusion of moderate stringency hybridization conditions in claim 1, said claim encompasses numerous polynucleotides which may

completely unrelated to the polynucleotide of SEQ ID NO:2, 16 and 18 encoding the polypeptide of SEQ ID Nos: 2, 17 and 19. Applicant has not disclosed how to use said sequences.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
May 6, 2002 NSB

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER